Claim 1 was rejected under 35 U.S.C. § 102(b) as being anticipated by Song et al.

Song et al. do not teach any physiological activity or biological activity of the peptide, the receptor variants or receptor antagonists. Song et al. teaches only that the peptide **may** have functional importance. No disclosure nor data is presented that demonstrates physiological activity.

Additionally, Song et al. only teach a potential functional importance of the peptide in context to the entire receptor, not as a stand-alone peptide. This is underscored by the following disclosure:

> Alternative splicing occurs in the third intracellular loop of certain other G protein-coupled receptors, such as the number D_2 and D_3 dopamine receptors (21-23). In the case of the D_2 and D_3 dopamine receptor, alternative splicing may affect the ***coupling of the receptor*** to second-messenger pathways (24, 25). ***Thus***, the pentapeptide cassette in the gastrin/CCK_B receptor may be of potential functional importance.
>
> (page 9088, col. 2, 3rd ¶ - page 9089, col. 1, 1st ¶.)

Thus, any potential physiological importance is discussed in the context of the effect it would have on how the gastrin/CCK_B **receptor** may function or interact as other G protein-coupled receptors function. Song et al. do not even hint that the identified protein sequence can have physiological activity as a stand-alone peptide. The claims as amended require that the peptide sequence have physiological activity as a stand-alone peptide. Because Song et al. do not satisfy this element, this reference cannot anticipate the claims.

Nor do Song et al. teach "a substance or cell present *in vivo* that acts as an antagonist to the ligand for the receptor or to the cell which expresses the receptor of the ligand." Applicant respectfully requests that the Examiner identify where in Song et al. this element is disclosed. Applicant respectfully submits that both the amendments and the

arguments distinguish claim 1 and its dependent claims over the cited reference. As such, this § 102(b) rejection should be withdrawn.

Claims 1-4 and 18 were rejected under 354 U.S.C. § 103(a) as being unpatentable over Song et al. in view of Olsson et al. As discussed above, Song et al. did not teach any physiological activity or biological activity of the peptide, the receptor variants or receptor antagonists. Song et al. teaches only that the peptide may have functional importance. Additionally, Song et al. only teach a potential functional importance of the peptide in the context of the entire receptor, not as a stand-alone peptide. Finally, Song et al. do not teach "a substance or cell present in vivo that acts as an antagonist for the receptor or to the cell which expresses the receptor at the ligand."

Nor does Olsson et al. teach "a substance or cell present in vivo that acts as an antagonist for the receptor or to the cell which expresses the receptor." Applicant respectfully requests that Examiner identify any disclosure of this element in Olsson et al. Thus, because neither Song nor Olsson disclose this limitation, they cannot render the claims obvious in combination.

It is Examiner's assertion that Olsson et al. teach "a method for determining and producing biologically active peptides wherein . . . the method comprises receptor variance shorter (deleted or missing region) as compared to wild-type sequences (see Col. 12, lines 57-67, and Col. 13, lines 1-48)." It is respectfully submitted that this is taught nowhere in the Olsson reference. Olsson nowhere teaches the comparison of two receptor variants to identify a missing or deleted region. Olsson et al. teach that "activation sequences" are identified by their homology to MHC Class I antigens. (Col. 9, l. 44 - Col. 10, l. 42.) Thus, any bioactivity disclosed by Olsson et al. is limited to peptides with sequence homology to MHC-I. The only express motivation provided by Olsson et al. is identifying receptor-specific sites of importance ***as evidenced by their homology to MHC-1***. Thus, an ordinary practitioner would only have been motivated to analyze peptides that had significant homology to MHC-1, not any peptide sequence that may be a part of the receptor.

Thus, there is no express motivation to combine these references. Indeed, Olsson actually teaches away from analyzing any sequences that do not have homology to MHC-I. It is respectfully submitted that the rejection of the claims cannot be maintained over the references, as none of the references teach or suggest the subject matter of these claims.

Applicant submits that the claims are now in condition for allowance, and respectfully request a notice to that effect. If the Examiner believes any further discussion will advance the prosecution of the application, she is highly encouraged to telephone Applicant's attorney at the number given below. Applicant believes that no fees are necessary at this time. If Applicant is mistaken, please charge any additional fees or credit any overpayments as a result of the filing of this paper to our Deposit Account No. 02-3978 — a duplicate of this paper is enclosed for that purpose.

Respectfully submitted,

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By _____
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Date: ***July 17, 2002***

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Attachment

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Twice Amended) A method for the identification of isolated physiologically active peptides, the method comprising the steps of:

comparing the cDNA sequences of receptor variants of receptors having one or more variants in size, the receptors being receptive of an identical ligand and being products of the same gene, wherein there is a substance or cell present in vivo that acts as an antagonist to the ligand for the receptor or to [having a functional antagonism against the ligand for the receptor or against] the cell which expresses the receptor of the ligand; [and]

identifying which cDNA sequence in the larger receptor is missing in the shorter receptor[.]; and

determining the corresponding peptide sequence from the cDNA sequence of the missing region, wherein said peptide sequence of the missing domain has physiological activity as a stand-alone peptide irrespective of its activity as part of a receptor.

2. (Twice Amended) A method of producing isolated physiologically active peptides, wherein the missing region determined by the method of claim 1 is produced.